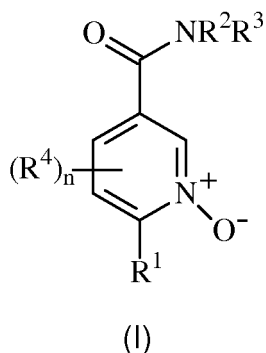


Application No.: 10/781,340  
 Attorney Docket No.: 60117-106  
 First Applicant's Name: Neil S. Cutshall  
 Application Filing Date: February 17, 2004  
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## AMENDMENT TO THE CLAIMS

1. (Withdrawn) A compound having the structure (I):



and optical isomers, diastereomers, enantiomers and pharmaceutically acceptable salts thereof, wherein

$R^1$  is selected from  $R^5$  and  $R^5$ -( $C_1$ - $C_6$ heteroalkylene)- where  $R^5$  is selected from hydrogen, halogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring and heterocycle aliphatic ring, amino or hydroxy;

$R^2$  and  $R^3$  are independently hydrogen, alkyl, heteroalkyl, aryl, aryl(alkylene), heteroaryl, heteroaryl(alkylene), carbocycle, carbocycle(alkylene), heterocycle, and heterocycle(alkylene);

each occurrence of  $R^4$  is independently selected from halogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring and heterocycle aliphatic ring, amino or hydroxy; and

Application No.: 10/781,340  
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n is 0, 1, 2 or 3.

2. (Withdrawn) A compound of claim 1 wherein n is 0.

3. (Withdrawn) A compound of claim 1 wherein n is 1.

4. (Withdrawn) A compound of claim 1 wherein n is 0 or 1 and R<sup>2</sup> is H.

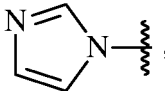
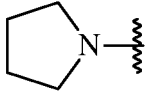
5. (Withdrawn) A compound of claim 4 wherein R<sup>1</sup> is R<sup>5</sup>-SO<sub>2</sub><sup>-</sup> and R<sup>5</sup> is selected from alkyl, heteroalkyl, aryl, carbocycle, aryl(alkylene), and carbocycle(alkylene).

6. (Withdrawn) A compound of claim 5 wherein, for R<sup>5</sup>, alkyl is C<sub>1</sub>-C<sub>10</sub>alkyl; heteroalkyl is C<sub>1</sub>-C<sub>10</sub>alkyl with 1, 2 or 3 heteroatoms selected from N, O and S; aryl is phenyl, substituted phenyl, naphthyl or substituted naphthyl; carbocycle is C<sub>3</sub>-C<sub>8</sub>carbocycle; and alkylene is C<sub>1</sub>-C<sub>10</sub>alkylene.

7. (Withdrawn) A compound of claim 5 wherein R<sup>1</sup> is selected from (C<sub>1</sub>-C<sub>6</sub>alkyl)SO<sub>2</sub><sup>-</sup>, PhSO<sub>2</sub><sup>-</sup>, fluorinatedphenylSO<sub>2</sub><sup>-</sup>, PhCH<sub>2</sub>SO<sub>2</sub><sup>-</sup>, cyclopentylSO<sub>2</sub><sup>-</sup>, *m*-carboxyphenylSO<sub>2</sub><sup>-</sup>, *m*-methylphenylSO<sub>2</sub><sup>-</sup>, and HOOC-(C<sub>1</sub>-C<sub>4</sub>alkylene)SO<sub>2</sub><sup>-</sup>.

8. (Withdrawn) A compound of claim 1 wherein R<sup>1</sup> is selected from halogen, amino, hydrocarbylamino, dihydrocarbylamino, hydrocarbyloxy, hydrocarbylthio, heterocyclyl, (heteroalkyl)amino, and (heteroaryl)amino.

Application No.: 10/781,340  
Attorney Docket No.: 60117-106  
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Examiner: Rita J. Desai

9. (Withdrawn) A compound of claim 7 wherein R<sup>1</sup> is selected from amino, (C<sub>1</sub>-C<sub>6</sub>alkyl)(C<sub>1</sub>-C<sub>6</sub>alkyl)amino, PhNH-, PhCH<sub>2</sub>NH-, , , and HOCH<sub>2</sub>CH<sub>2</sub>NH-.

10. (Withdrawn) A compound of claim 8 wherein R<sup>1</sup> is selected from halide and (C<sub>1</sub>-C<sub>6</sub>alkyl)S-.

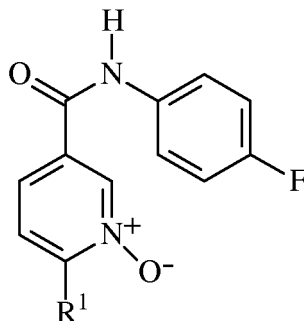
11. (Withdrawn) A compound of claim 10 wherein R<sup>1</sup> is chloride.

12. (Withdrawn) A compound of claim 4 wherein R<sup>3</sup> is selected from aryl, aryl(alkylene), heteroaryl, and heteroaryl(alkylene).

13. (Withdrawn) A compound of claim 12 wherein R<sup>3</sup> is aryl.

Application No.: 10/781,340  
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Examiner: Rita J. Desai

14. (Withdrawn) A compound of claim 1 having structure (II)



(II).

15. (Withdrawn) A compound of claim 14 wherein R<sup>1</sup> is selected from (C<sub>1-6</sub>alkyl)SO<sub>2</sub><sup>-</sup>, PhSO<sub>2</sub><sup>-</sup>, fluorinatedphenylSO<sub>2</sub><sup>-</sup>, PhCH<sub>2</sub>SO<sub>2</sub><sup>-</sup>, cyclopentylSO<sub>2</sub><sup>-</sup>, *m*-carboxyphenylSO<sub>2</sub><sup>-</sup>, *m*-methylphenylSO<sub>2</sub><sup>-</sup>, and HOOC-(C<sub>1</sub>-C<sub>4</sub>alkylene)SO<sub>2</sub><sup>-</sup>.

16. (Withdrawn) A compound of claim 4 wherein R<sup>3</sup> is benzyl or phenyl, the benzyl or phenyl having 0, 1, 2, 3 or 4 substituents selected from alkoxy, alkoxy carbonyl, alkyl, alkylamido, alkylcarbonyl, amido, benzyl optionally substituted with halogen, benzyloxy, carboxy, cyano, dialkylamido, haloalkyl, haloalkyloxy, halogen, hydroxy, nitro, oxoalkyl, phenyl optionally substituted with halogen, thioalkyl, thiocyanate, and thiohaloalkyl.

17. (Withdrawn) A compound of claim 1 wherein R<sup>3</sup> is selected from cycloalkyl, cycloalkyl(alkylene), cycloalkyl(heteroalkylene), heterocycloalkyl, heterocycloalkyl(alkylene), heterocycloalkyl(heteroalkylene), heteroaryl, heteroaryl(alkylene), and heteroaryl(heteroalkylene).

Application No.: 10/781,340  
Attorney Docket No.: 60117-106  
First Applicant's Name: Neil S. Cutshall  
Application Filing Date: February 17, 2004  
Office Action Dated: September 6, 2007  
Date of Original Response: December 4, 2007  
Date of Current Resubmission: April 9, 2008  
Examiner: Rita J. Desai

18. (Withdrawn) A compound of claim 1 wherein said compound is 6-Chloro-N-(4-fluoro-phenyl)-1-oxy-nicotinamide.
19. (Withdrawn) A compound of claim 1 wherein said compound is N-(4-Fluoro-phenyl)-6-(2-hydroxy-ethylamino)-1-oxy-nicotinamide.
20. (Withdrawn) A compound of claim 1 wherein said compound is 6-Bromo-N-(4-fluoro-phenyl)-1-oxy-nicotinamide.
21. (Withdrawn) A compound of claim 1 wherein said compound is 5,6-Dichloro-N-(4-fluoro-phenyl)-1-oxy-nicotinamide.
22. (Withdrawn) A compound of claim 1 wherein said compound is 6-Ethanesulfonyl-N-(4-fluoro-phenyl)-1-oxy-nicotinamide.
23. (Withdrawn) A compound of claim 1 wherein said compound is N-(4-Fluoro-phenyl)-1-oxy-6-(propane-2-sulfonyl)-nicotinamide.
24. (Withdrawn) A compound of claim 1 wherein said compound is N-(4-Fluoro-phenyl)-6-methanesulfonyl-1-oxy-nicotinamide.
25. (Withdrawn) A compound of claim 1 wherein said compound is 6-Benzenesulfonyl-N-(4-fluoro-phenyl)-1-oxy-nicotinamide.

Application No.: 10/781,340  
Attorney Docket No.: 60117-106  
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Date of Original Response: December 4, 2007  
Date of Current Resubmission: April 9, 2008  
Examiner: Rita J. Desai

26. (Withdrawn) A compound of claim 1 wherein said compound is N-(4-Fluoro-phenyl)-1-oxy-6-phenylmethanesulfonyl-nicotinamide.

27. (Withdrawn) A compound of claim 1 wherein said compound is 6-Chloro-N-(3-chloro-4-fluoro-phenyl)-1-oxy-nicotinamide.

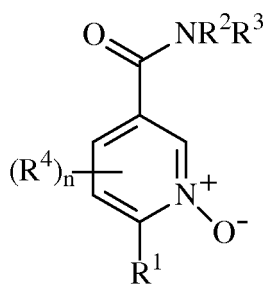
28. (Withdrawn) A compound of claim 1 wherein said compound is 6-Chloro-N-(4-iodo-phenyl)-1-oxy-nicotinamide.

29. (Withdrawn) A compound of claim 1 wherein  $R^1$  is selected from halogen, heteroalkyl or amino,  $R^2$  is H,  $R^3$  is aryl and  $R^4$  is H.

30. (Withdrawn) A composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier, adjuvant or incipient.

31. (Currently Amended) A method for antagonizing chemokine receptors comprising administering to a patient in need thereof an effective amount of a compound having the structure (I):

Application No.: 10/781,340  
 Attorney Docket No.: 60117-106  
 First Applicant's Name: Neil S. Cutshall  
 Application Filing Date: February 17, 2004  
 Office Action Dated: September 6, 2007  
 Date of Original Response: December 4, 2007  
 Date of Current Resubmission: April 9, 2008  
 Examiner: Rita J. Desai



(I)

and optical isomers, diastereomers, enantiomers and pharmaceutically acceptable salts thereof, wherein

R<sup>1</sup> is selected from hydrogen, halogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring and heterocycle aliphatic ring, amino or hydroxy;

R<sup>2</sup> is hydrogen; and

R<sup>3</sup> ~~are independently~~ is selected from ~~hydrogen, alkyl, heteroalkyl, aryl, and aryl(alkylene), heteroaryl, heteroaryl(alkylene), carbocycle, carbocycle(alkylene), heterocycle, and heterocycle(alkylene);~~

each occurrence of R<sup>4</sup> is independently selected from halogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring and ~~heterocycle aliphatic ring~~, amino or hydroxy; and

n is 0, or 1, ~~2 or 3~~.

32. (Original) A method for inhibiting a chemokine-mediated cellular event comprising administering to a patient in need thereof an effective amount of a compound of claim 31.

Application No.: 10/781,340  
Attorney Docket No.: 60117-106  
First Applicant's Name: Neil S. Cutshall  
Application Filing Date: February 17, 2004  
Office Action Dated: September 6, 2007  
Date of Original Response: December 4, 2007  
Date of Current Resubmission: April 9, 2008  
Examiner: Rita J. Desai

33. (Original) A method of claim 32 wherein the compound inhibits IL-8 and or GRO- $\alpha$  driven neutrophil chemotaxis.

34. (Original) The method of claim 32 wherein the compound inhibits a CXCR1 receptor.

35. (Original) The method of claim 32 wherein the compound inhibits a CXCR2 receptor.

36. (Original) The method of claim 32 for the treatment of a disorder selected from Inflammatory Bowel Disease (IBD), psoriasis, rheumatoid arthritis, Acute Respiratory Distress Syndrome (ARDS), cancer, atherosclerosis, reperfusion injury, and graft vs. host disease.

37. (Currently Amended) A method for inhibiting a G-protein-coupled, seven-transmembrane domain (7TM) receptor in a patient comprising administering to the patient a compound of claim 431 in an amount effective to inhibit the receptor.

38. (Original) A method of claim 37 wherein the compound modulates the binding of Peptide YY (PYY) to a NPY cell receptor.

39. (Original) A method of claim 37 wherein the compound modulates the binding of somatostatin to a somatostatin cell receptor.



Application No.: 10/781,340  
Attorney Docket No.: 60117-106  
First Applicant's Name: Neil S. Cutshall  
Application Filing Date: February 17, 2004  
Office Action Dated: September 6, 2007  
Date of Original Response: December 4, 2007  
Date of Current Resubmission: April 9, 2008  
Examiner: Rita J. Desai

40. (Original) A method of claim 37 wherein the compound modulates the binding of MIP-1 $\beta$  to a CCR5 cell receptor.

41. (Currently Amended) A method for treating an inflammation event, comprising administering to a patient in need thereof, through a therapeutically or prophylactically acceptable manner, a therapeutically or pharmaceutically effective amount of the compound of claim 314.

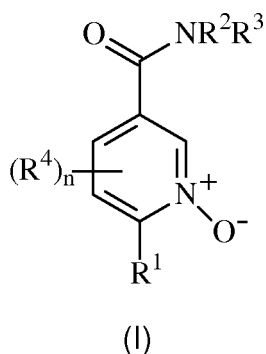
42. (Original) The method of claim 41 wherein administration is selected from transdermal, oral, intravenous, intramuscular, vaginal, rectal, pulmonary, subcutaneous, sublingual and transmucosal administration.

43. (Withdrawn) A method for identifying a binding partner to a compound of claim 1 comprising:  
immobilizing proteins known to be involved in the TNF- $\alpha$  signaling pathway onto a suitable carrier; and  
passing a solution of said compounds in isolation or mixture over said proteins and analyzing for compound:protein complex formation using surface plasmon resonance (SPR).

Application No.: 10/781,340  
Attorney Docket No.: 60117-106  
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Application Filing Date: February 17, 2004  
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Date of Original Response: December 4, 2007  
Date of Current Resubmission: April 9, 2008  
Examiner: Rita J. Desai

44. (Withdrawn) A method for identifying a binding partner to a compound of claim 1 comprising:  
providing said compound(s) bound to a solid support to provide solid phase compounds;  
contacting a cell or cell components with said solid phase compounds in isolation or mixture;  
removing uncomplexed cellular material, for example by gentle washing with aqueous buffer; and  
recovering said binding partner from the solid phase compounds.

45. (New) A method for antagonizing a chemokine receptor selected from the group consisting of: IL-8, GRO- $\alpha$ , MIP-1 $\alpha$ , MIP-1 $\beta$ , RANTES, CXCR1, CXCR2, CXCR4, and CCR5, comprising administering to a patient in need thereof an effective amount of a compound having the structure (I):



and optical isomers, diastereomers, enantiomers and pharmaceutically acceptable salts thereof, wherein

Application No.: 10/781,340  
Attorney Docket No.: 60117-106  
First Applicant's Name: Neil S. Cutshall  
Application Filing Date: February 17, 2004  
Office Action Dated: September 6, 2007  
Date of Original Response: December 4, 2007  
Date of Current Resubmission: April 9, 2008  
Examiner: Rita J. Desai

$R^1$  is selected from hydrogen, halogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring and heterocycle aliphatic ring, amino or hydroxy;

$R^2$  is hydrogen;

$R^3$  is selected from aryl, and aryl(alkylene);

each occurrence of  $R^4$  is independently selected from halogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring and amino or hydroxy; and

n is 0, 1, 2 or 3.

46. A method for inhibiting a chemokine-mediated cellular event comprising administering to a patient in need thereof an effective amount of a compound of claim 45.